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=> d his

     (FILE 'HOME' ENTERED AT 18:54:03 ON 28 DEC 2007)
     FILE 'REGISTRY' ENTERED AT 18:54:28 ON 28 DEC 2007
L1      17 S (AMPRENAVIR OR INDINAVIR OR NELFINAVIR OR RITONAVIR OR SAQUINAVIR
           OR LOPINAVIR OR ABACAVIR OR DIDANOSINE OR LAMIVUDINE OR STAVUDINE
           OR ZALCITABINE OR ZIDOVUDINE OR DELAVIRDINE OR EFAVIRENZ OR
           NEVIRAPINE OR TANOFAVIR OR ATAZANAVIR OR PEPTIDE T OR T-20)/CN
     FILE 'CA' ENTERED AT 18:57:07 ON 28 DEC 2007
L2   18404 S L1 OR AMPRENAVIR OR INDINAVIR OR NELFINAVIR OR RITONAVIR OR
           SAQUINAVIR OR LOPINAVIR OR ABACAVIR OR DIDANOSINE OR LAMIVUDINE OR
           STAVUDINE OR ZALCITABINE OR ZIDOVUDINE OR DELAVIRDINE OR EFAVIRENZ
           OR NEVIRAPINE OR TANOFAVIR OR ATAZANAVIR OR PEPTIDE T OR T-20
L3    4903 S (STAVIR OR SANILVUDINE OR DIDEOXYCYTIDINE OR AZITIDIN OR AZT OR
           TIMAZID OR VIDEX OR VIRAMUNE OR ZEFFIX OR ZEFIX OR LAMIVIR OR
           HEPTOVIR OR EPIVIR OR ZIAGEN OR COMPOUND J OR SUSTIVA OR STOCRIN
           OR NORVIR OR SAMPRENAVIR OR PROZEI OR ANGENERASE OR AGENERASE OR
           KOLETRA OR ALUVIRAN OR REYATAZ)
L4  270452 S MASS SPECTRO?
L5    8629 S ANTIRETROVIRAL? OR ANTI RETROVIRAL?
L6      76 S L4 AND L5
L7     319 S L4 AND L2-3
L8     296 S L4 AND DEPROTEIN?
L9     132 S L8 AND (ACETONITRILE OR ETOH OR ETHANOL OR METHANOL OR MEOH)
L10      2 S L7 AND L9
L11  18058 S (HIV OR AIDS)(4A)(DRUG OR TREATMENT OR THERAPY OR PHARMACEUTICAL)
L12    108 S L4 AND L11
L13     51 S L11 AND L7
L14    161 S L6,L10,L12-13
L15    102 S L9 AND (LIQUID(1A)CHROMATOG? OR HPLC)
L16     16 S L9 AND CENTRIF?
L17     65 S L15 AND(STANDARD OR CONTROL)
L18     70 S L16-17
     FILE 'CA' ENTERED AT 19:36:50 ON 28 DEC 2007
L19     76 S L14 AND PY<2004
L20      7 S L14 AND PATENT/DT AND PY<2006
     FILE 'BIOSIS' ENTERED AT 19:38:32 ON 28 DEC 2007
L21     73 S L19
     FILE 'MEDLINE' ENTERED AT 19:39:19 ON 28 DEC 2007
L22     74 S L19
     FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 19:40:29 ON 28 DEC 2007
L23    188 DUP REM L18 L19 L20 L21 L22 (112 DUPLICATES REMOVED)

=> d bib,ab l23 1-188

L23  ANSWER 40 OF 188  CA  COPYRIGHT 2007 ACS on STN
AN   141:343434  CA
TI   Anti-retroviral analysis by mass spectrometry
IN   Soldin, Steven J.
PA   Georgetown University, USA; Children's National Medical Center
SO   PCT Int. Appl., 40 pp.
PI   WO 2004089182        A2    20041021    WO 2004-IB1337          20040401
     US 2005032042        A1    20050210    US 2004-814244          20040401
PRAI US 2003-462672P      P     20030414
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AB Methods for the simultaneous or sequential anal. and quantification of a plurality of **antiretroviral** analytes in a complex biol. matrix by **mass spectrometry** are disclosed. The methods require minimal sample size, minimal prepn. time and allow for rapid through-put. The system is particularly useful in therapeutic drug monitoring.

L23 ANSWER 63 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 140:70198 CA
TI Improved method for concurrent quantification of **antiretrovirals** by liquid chromatography-tandem **mass spectrometry**
AU Ghoshal, Amit K.; Soldin, Steven J.
CS Department of Laboratory Medicine, Children's National Medical Center, Washington, DC, USA
SO Therapeutic Drug Monitoring (**2003**), 25(5), 541-543
AB Therapeutic drug monitoring (TDM) is becoming more widespread to optimize the **treatment** of patients with **HIV/AIDS**. The analytic component of TDM requires a drug assay with high specificity, small sample vol. requirements, reasonable cost, and rapid turnaround time. This study modified a procedure for the concurrent measurement of 15 **antiretrovirals** by tandem **mass spectrometry**. The upper limit of the calibration curves was extended to 10,000 ng/mL, and the matrix for stds. was changed from MeOH to serum. Also, an addnl. drug, tenofovir, a nucleotide reverse transcription inhibitor, was included in the revised/improved method. Calibration curves showed good linearity between a concn. range of 100 and 10,000 ng/mL ($r > 0.997$ for all drugs). Accuracy was assessed by correlation of the calibrators with proficiency testing samples spiked with known drug concns. and yielded results within 8% of the target values.

L23 ANSWER 70 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 139:254 CA
TI Rapid quantification of HIV protease inhibitors in human plasma by high-performance liquid chromatography coupled with electrospray ionization tandem **mass spectrometry**
AU Crommentuyn, K. M. L.; Rosing, H.; Nan-Offeringa, L. G. A. H.; Hillebrand, M. J. X.; Huitema, A. D. R.; Beijnen, J. H.
CS Department of Pharmacy and Pharmacology, Slotervaart Hospital, Amsterdam, 1066 EC, Neth.
SO Journal of Mass Spectrometry (**2003**), 38(2), 157-166
AB HIV protease inhibitors are important **antiretroviral** drugs which have substantially reduced the morbidity and mortality assocd. with HIV-1 infection. Recent data have shown relationship between plasma concns. of the protease inhibitors and clin. response, which makes therapeutic drug monitoring valuable. We have developed and validated an assay, using liq. chromatog. coupled with electrospray tandem **mass spectrometry** (LC/MS/MS), for the routine quantification of the six licensed protease inhibitors (amprenavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir) and the pharmacol. active nelfinavir metabolite M8 in plasma. The sample pretreatment consisted of protein pptn. with a mixt. of methanol and acetronitrile using only 100 μl of plasma. Chromatog. sepn. was performed on an Inertsil ODS3 column (50 × 2.0 mm i.d.,

particle size 5 μm), with a quick stepwise gradient using an acetate buffer (pH 5) and methanol, at a flow rate of 0.5 mL min-1. The anal. run time was 5.5 min. The use of a 96-well plate autosampler allowed batch sizes up to 150 patient samples. The triple-quadrupole **mass spectrometer** was operated in the pos. ion mode and multiple reaction monitoring was used for drug quantification. The method was validated over the concn. ranges 0.01-10 μg ml-1 for indinavir and saquinavir, 0.1-10 μg ml-1 for amprenavir, 0.05-10 μg ml-1 for nelfinavir and ritonavir, 0.1-20 μg ml-1 for lopinavir and 0.01-5 μg ml-1 for M8. Saquinavir-d5 and indinavir-d6 were used as internal stds. The coeffs. of variation were always <10% for both intra-day and inter-day precisions for each compd. Mean accuracies were also between the designated limits (±15%). The validated concn. ranges proved to be adequate in daily practice. This robust and fast LC/MS/MS assay is now successfully applied for routine therapeutic drug monitoring and pharmacokinetic studies in our hospital.

L23 ANSWER 86 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 138:265072 CA
TI Determination of **Lamivudine/stavudine/Efavirenz** in human serum using liquid chromatography/electrospray tandem **mass spectrometry** with ionization polarity switch
AU Fan, Bin; Bartlett, Michael G.; Stewart, James T.
CS Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA, 30602-2352, USA
SO Biomedical Chromatography (**2002**), 16(6), 383-389
AB A high-performance liq. chromatog./tandem **mass spectrometry** (LC-MS-MS) method with ionization polarity switch was developed and validated in human serum for the detn. of a **Lamivudine** (3TC)/**stavudine** (d4T)/**Efavirenz** combination **HIV therapy**. Solid-phase extn. (SPE) was used to ext. these anti-**HIV drugs** and internal std. aprobarbital. A gradient mobile phase consisting of acetonitrile and 20 mM ammonium acetate buffer with pH adjusted to 4.5 using glacial acetic acid was utilized to sep. these drugs on a Hexylsilane column (150 × 2.0 mm i.d.). The total run time between injections was 18 min. The precursor and major product ions of these drugs were monitored on a triple quadrupole **mass spectrometer** in the multiple reactions monitoring (MRM) mode. Ionization polarity was switched in the middle of the LC run allowing these anti-**HIV drugs** with different physicochem. properties to be detected simultaneously. The effect of ion suppression from human serum was studied and no interference with the anal. was noted. The method was validated over the range of 1.1-540 ng/mL for 3TC, 12.5-6228 ng/mL for d4T, and 1.0-519 ng/mL for **Efavirenz**. The method was shown to be accurate, with intra-day and inter-day accuracy <14.0% and precise, with intra-day and inter-day precision <13.1%. The extn. recoveries of all analytes were >90%.

L23 ANSWER 93 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 138:49313 CA

TI Simple rapid method for quantification of **antiretrovirals** by liquid chromatography-tandem **mass spectrometry**

AU Volosov, Andrew; Alexander, Christopher; Ting, Lillian; Soldin, Steven J.

CS Children's National Medical Center, Washington, DC, USA

SO Clinical Biochemistry (**2002**), 35(2), 99-103

AB A simple, fast and universal method was developed for quantification of any combination of all 15 currently marketed anti-**HIV drugs** in human plasma, using a liq. chromatog.-tandem **mass spectrometry**. An 80-μL plasma sample was spiked with internal std. (cimetidine), and protein was pptd. with 200 μL MeCN. The sample was centrifuged and 30 μL aliquot was injected onto the HPLC column, where it underwent an online extn. with NH4OAc. The automatic switching valve was then activated, changing the mobile phase to MeOH and thereby eluting the analytes into the tandem **mass spectrometer**. **Stavudine**, **zidovudine** (**AZT**) and **efavirenz** were analyzed in the neg. mode, while all the other drugs were analyzed in the pos. mode. The high selectivity of a tandem mass analyzer allowed detn. of any combination of the drugs within a 4.5-min run. Between-day precision was <10% for all the analytes at the concns. tested. Accuracy ranged 95%-105%. The method was linear over the measuring ranges of all the analytes. Within-run precision gave a coeff. of variation of <7% for all the analytes. Good correlation with other anal. methods was obsd. The simplicity, universality and high throughput of the method make it suitable for application in a clin. lab.

L23 ANSWER 97 OF 188 CA COPYRIGHT 2007 ACS on STN

AN 137:210460 CA

TI Pharmacokinetics of plasma enfuvirtide after subcutaneous administration to patients with human immunodeficiency virus: inverse Gaussian density absorption and 2-compartment disposition

AU Zhang, Xiaoping; Nieforth, Keith; Lang, Jean-Marie; Rouzier-Panis, Regine; Reynes, Jacques; Dorr, Albert; Kolis, Stanley; Stiles, Mark R.; Kinchelow, Tosca; Patel, Indravadan H.

CS Department of Clinical Pharmacology, Hoffman-La Roche Inc, Nutley, USA

SO Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (**2002**), 72(1), 10-19

AB Objective: Enfuvirtide (**T-20**) is the first of a novel class of human immunodeficiency virus (**HIV**) **drugs** that block gp41-mediated viral fusion to host cells. The objectives of this study were to develop a structural pharmacokinetic model that would adequately characterize the absorption and disposition of enfuvirtide pharmacokinetics after both i.v. and s.c. administration and to evaluate the dose proportionality of enfuvirtide pharmacokinetic parameters at a s.c. dose higher than that currently used in phase III studies. Metbods: Twelve patients with HIV infection received 4 single doses of enfuvirtide sepd. by a 1-wk washout period in an open-label, randomized, 4-way crossover fashion. The doses studied were 90 mg (i.v.) and 45 mg, 90 mg, and 180 mg (s.c.). Serial blood samples were collected up to 48 h after each dose. Plasma enfuvirtide concns. were measured with use of a validated liq. chromatog.-tandem **mass spectrometry** method. Results: Enfuvirtide plasma concn.-time data after s.c. administration were well described by an

inverse Gaussian d. function-input model linked to a 2-compartment open distribution model with first-order-elimination from the central compartment. The model-derived mean pharmacokinetic parameters (±SD) were vol. of distribution of the central compartment (3.8 ± 0.8 L), vol. of distribution of the peripheral compartment (1.7 ± 0.6 L), total clearance (1.44 ± 0.30 L/h), intercompartmental distribution (2.3 ± 1.1 L/h), bioavailability (89% ± 11%), and mean absorption time (7.26 h, 8.65 h, and 9.79 h for the 45-mg, 90-mg, and 180-mg dose groups, resp.). The terminal half-life increased from 3.46 to 4.35 h for the s.c. dose range from 45 to 180 mg. Conclusions: An inverse Gaussian d. function-input model linked to a 2-compartment open distribution model with first-order elimination from the central compartment was appropriate to describe complex absorption and disposition kinetics of enfuvirtide plasma concn.-time data after s.c. administration to patients with HIV infection. Enfuvirtide was nearly completely absorbed from s.c. depot, and pharmacokinetic parameters were linear up to a dose of 180 mg in this study.

L23 ANSWER 102 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 135:55430 CA
TI Circulating metabolites of the human immunodeficiency virus protease inhibitor **nelfinavir** in humans: structural identification, levels in plasma, and antiviral activities
AU Zhang, Kanyin E.; Wu, Ellen; Patick, Amy K.; Kerr, Bradley; Zorbas, Mark; Lankford, Angela; Kobayashi, Takuo; Maeda, Yuki; Shetty, Bhasker; Webber, Stephanie
CS Pfizer Global Research and Development, La Jolla, CA, USA
SO Antimicrobial Agents and Chemotherapy (**2001**), 45(4), 1086-1093
AB **Nelfinavir** mesylate (Viracept, formally AG1343) is a potent and orally bioavailable human immunodeficiency virus (HIV) type 1 (HIV-1) protease inhibitor (Ki = 2 nM) and is being widely prescribed in combination with HIV reverse transcriptase inhibitors for the **treatment** of **HIV** infection. The current studies evaluated the presence of metabolites circulating in plasma following the oral administration of **nelfinavir** to healthy volunteers and HIV-infected patients, as well as the levels in plasma and antiviral activities of these metabolites. The results showed that the parent drug was the major circulating chem. species, followed in decreasing abundance by its hydroxy-t-butylamide metabolite (M8) and 3'-methoxy-4'-hydroxynelfinavir (M1). Antiviral assays with HIV-1 strain RF-infected CEM-SS cells showed that the 50% effective concns. (EC50) of **nelfinavir**, M8, and M1 were 30, 34, and 151 nM, resp., and that the corresponding EC50 against another HIV-1 strain, IIIB, in MT-2 cells were 60, 86, and 653 nM. Therefore, apparently similar in vitro antiviral activities were demonstrated for **nelfinavir** and M8, whereas an approx. 5- to 11-fold-lower level of antiviral activity was obsd. for M1. The active metabolite, M8, showed a degree of binding to human plasma proteins similar to that of **nelfinavir** (98%). Concns. in plasma of **nelfinavir** and its metabolites in 10 **HIV**-pos. patients receiving **nelfinavir therapy** (750 mg three times per day) were detd. by a liq. chromatog. tandem **mass spectrometry** assay. At steady state (day 28),

the mean plasma **nelfinavir** concns. ranged from 1.73 to 4.96 μM and the M8 concns. ranged from 0.55 to 1.96 μM, whereas the M1 concns. were low and ranged from 0.09 to 0.19 μM. In conclusion, the findings from the current studies suggest that, in humans, **nelfinavir** forms an active metabolite circulating at appreciable levels in plasma. The active metabolite M8 may account for some of the antiviral activity assocd. with **nelfinavir** in the **treatment** of **HIV** disease.

L23 ANSWER 111 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 136:318752 CA
TI **Antiretrovirals**: simultaneous determination of five protease inhibitors and three nonnucleoside transcriptase inhibitors in human plasma by a rapid high-performance liquid chromatography-**mass spectrometry** assay
AU Villani, Paola; Feroggio, Marina; Gianelli, Luca; Bartoli, Antonella; Montagna, Michela; Maserati, Renato; Regazzi, Mario B.
CS Department of Pharmacology, Universita di Pavia, Pavia, 27100, Italy
SO Therapeutic Drug Monitoring (**2001**), 23(4), 380-388
AB An anal. technique using liq. chromatog. (LC) coupled with electrospray-**mass spectrometry** (ESI-MS) has been developed for the simultaneous detn. of five protease inhibitors (PIs): saquinavir, indinavir, ritonavir, nelfinavir, and amprenavir; and three non-nucleoside reverse transcriptase inhibitors (NNRTIs): nevirapine, delavirdine, and efavirenz, in human plasma. This assay allows the elution and identification of these drugs in a single run (10 min) using a linear gradient with water and acetonitrile. The procedure involves liq.-liq. extn. High-performance liq. chromatog. (HPLC) sepn. was achieved on a C18 reversed-phase column, with a linear gradient elution followed by **mass spectrometry** detection. The calibration curves, obtained by automatic process peak area integration, show a good linearity in a range of concns. between 20 and 10,000 ng/mL (40-10,000 ng/mL for efavirenz). The limit of detection was approx. 10 ng/mL for seven drugs (25 ng/mL for efavirenz). The coeffs. of variation (CV) were always less than 15% for both intra-day and inter-day precision for each compd. The recovery of the eight drugs ranged from 88.5% to 100%. This novel LC/ESI-MS assay provides an excellent method for simultaneous quant. monitoring of different components of the highly active **antiretroviral** treatments (HAARTs) in patients treated simultaneously with PIs and NNRTIs, and it has been successfully applied to therapeutic drug monitoring and pharmacokinetic studies.

L23 ANSWER 120 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 135:86476 CA
TI Liquid chromatographic-tandem **mass spectrometric** determination of amprenavir (agenerase) in serum/plasma of human immunodeficiency virus type-1 infected patients receiving combination **antiretroviral** therapy
AU Gunawan, S.; Griswold, M. P.; Kahn, D. G.
CS 7855 Haskell Avenue, Suite 302, Consolidated Laboratory Services, Van Nuys, CA, 91406-1902, USA
SO Journal of Chromatography, A (**2001**), 914(1-2), 1-4
AB A selective assay method for quantitation of amprenavir (agenerase) in human immunodeficiency virus type-1 infected patient serum or plasma

using liq. chromatog.-tandem **mass spectrometry** (LC-MS-MS) is described. Amprenavir and an internal std. (reserpine) are extd. by liq.-liq. extn. and chromatog. sepd. by a reversed-phase C18-anal. column. The triple quadrupole LC-MS-MS system is operated in the pos.-ion mode and multiple reaction monitoring was used for drug quantitation. The method was validated at 0.05-10.0 μg/mL. The RSDs for the intra-day and inter-day detns. ranged from 5.3 to 6.1% and from 4.7 to 6.2%, resp. The av. assay accuracy at two different concns. ranged from 96.0 to 103.0% and the extn. recovery of amprenavir was 90.8%. The lower limit of quantitation was 0.05 μg/mL. Using a short microbore column, the anal. was completed in <5 min.

L23 ANSWER 127 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 134:141289 CA
TI Simultaneous quantitation of the 5'-triphosphate metabolites of **zidovudine**, **lamivudine**, and **stavudine** in peripheral mononuclear blood cells of HIV infected patients by high-performance liquid chromatography tandem **mass spectrometry**
AU Moore, J. D.; Valette, G.; Darque, A.; Zhou, X.-J.; Sommadossi, J.-P.
CS Center for AIDS Research, Division of Clinical Pharmacology, University of Alabama at Birmingham, Birmingham, AL, USA
SO Journal of the American Society for Mass Spectrometry (**2000**), 11(12), 1134-1143
AB A high-performance liq. chromatog. (HPLC) method utilizing triple quadrupole **mass spectrometry** (MS) detection was developed and validated for the simultaneous measurement of the intracellular nucleoside 5'-triphosphate anabolites of **zidovudine** (ZDV-TP), **lamivudine** (3TC-TP), and **stavudine** (d4T-TP). These compds. were extd. from patient peripheral blood mononuclear cells (PBMCs) which are the sites of **HIV** replication and **drug** action. Ion-exchange solid phase extn. (SPE) followed by enzymic digestion with alk. phosphatase was utilized to yield the measurable nucleoside forms of the nucleotides. Reversed phase C-18 SPE with addn. of a nucleoside internal std., 3'-azido-2',3'-dideoxyuridine (AzdU) allowed for the indirect measurement of the original 5'-triphosphate concn. by HPLC/MS/MS. Quantitation was performed from calibration curves generated from authentic 5'-triphosphate stds. spiked in PBMCs from healthy volunteers. Anal. range for the three 5'-triphosphates was equiv. to 50-45,000 pg. Mean interassay accuracies for 3TC-TP, d4T-TP, and ZDV-TP (n > 90) were 99.4%, 100.1%, and 108.0%, resp. Mean interassay precisions (%C.V.) for 3TC-TP, d4T-TP, and ZDV-TP (n > 90) were 8.8%, 10.4%, and 8.2%, resp. Recovery of the extn. method was 79.2%, 83.1%, and 98.3% for 3TC-TP, d4T-TP, and ZDV-TP, resp. This method can be utilized to measure the intracellular 5'-triphosphate levels in **HIV** infected patients receiving **antiretroviral therapy** contg. the nucleoside reverse transcriptase inhibitors 3TC, d4T, or ZDV.

L23 ANSWER 142 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 132:65 CA
TI Analysis of cyclophosphamide and five metabolites from human plasma using **liquid chromatography-mass spectrometry** and gas chromatography-nitrogen-phosphorus detection
AU Kalhorn, Thomas F.; Ren, Song; Howald, William N.; Lawrence, Ross F.;

Slattery, John T.
CS Department of Pharmaceutics, University of Washington, Seattle, WA, 98195, USA
SO Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 732(2), 287-298
AB A combined GC and **HPLC**-MS assay for the quantification of cyclophosphamide (CY) and its 5 metabolites (dechloroethylcyclophosphamide, 4-oxocyclophosphamide, carboxyethylphosphoramide mustard, phosphoramide mustard, hydroxypropylphosphoramide mustard) in human blood plasma are presented. The procedure is adapted to the chem. properties of the compds. of interest. Non-polar compds. are extd. into methylene chloride, concd., and analyzed by GC-NPD after derivatization. The remaining aq. fraction is **deproteinated** with **acetonitrile-methanol** prior to sepn. by reversed-phase **HPLC** and detection using atm. pressure ionization MS. **Std.** curves were linear over the required range and reproducible over 5 mo. Plasma concn.-time profiles of CY and metabolites from a patient receiving CY by i.v. infusion are presented.

L23 ANSWER 150 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 131:82478 CA
TI Simultaneous determination of six protease/reverse transcriptase inhibitors in human plasma utilizing LC/MS/MS
AU Shoup, R. E.; Ren, Xiaoli; Johnson, Angela P.; Gray, Donald A.; Evarts, Simone; Gill, Lynn; Beato, Brian D.
CS BAS Analytics A Division of Bioanalytical Systems, Inc., West Lafayette, IN, 47906, USA
SO Current Separations (**1999**), 18(1), 17-22
AB With the success of "combination therapies" using reverse transcriptase inhibitors, antiinfectives, and protease inhibitors in the **treatment** of **HIV** infection, BAS Analytics developed a single method for profiling six protease/reverse transcriptase inhibitors in human plasma. The method utilizes robotic solid phase extn. at neutral pH and is generally applicable to all the analytes and their internal stds.

L23 ANSWER 153 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 130:133620 CA
TI Identification of drug metabolites in biological matrixes by intelligent automated liquid chromatography/tandem **mass spectrometry**
AU Lopez, Linda L.; Yu, Xiao; Cui, Donghui; Davis, Margaret R.
CS ThermoQuest Finnigan, San Jose, CA, 95134, USA
SO Rapid Communications in Mass Spectrometry (**1998**), 12(22), 1756-1760
AB A rapid and systematic strategy for the identification of drug metabolites in biol. matrixes based on liq. chromatog. - tandem **mass spectrometry** (LC/MS/MS) techniques was utilized for the identification of **drug** metabolites of the **HIV** protease inhibitor **Indinavir**. This strategy integrates intelligent real-time **mass spectrometry** with HPLC detection and a predictive strategy for detecting metabolites arising from common biotransformations, to rapidly elucidate structures of drug metabolites. Structures of metabolites generated from in vitro incubation mixts. of **Indinavir** were characterized from a single chromatog. anal. using the automated LC/MS/MS methodol., thus reducing data acquisition time and improving efficiency.

L23 ANSWER 155 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 129:41354 CA
TI Analysis of **antiretroviral** nucleosides by electrospray ionization **mass spectrometry** and collision induced dissociation
AU Font, Eva; Lasanta, Sonia; Rosario, Osvaldo; Rodriguez, Jose F.
CS Department of Chemistry, University of Puerto Rico, P. R.
SO Nucleosides & Nucleotides (**1998**), 17(5), 845-853
AB **Antiretroviral** nucleoside drugs used against the human immunodeficiency virus (HIV) infection have been analyzed using neg. ion electrospray ionization (ESI) **mass spectrometry** and collision-induced dissocn. (CID-MS/MS). Mass fragmentation of azidothymidine (AZT), didanosine (ddI), dideoxycytidine (ddC) and dideoxythiacytidine (3TC) were obtained at different cone voltages and collision energies. Fragmentation of purines and pyrimidines occurred by different pathways. For purines (ddI), the fragmentation was similar to those found in endogenous nucleosides; mainly the pseudo mol. ion is present (M-H)- and a cleavage through the glycosidic bond forming (B)- was obsd. For pyrimidines (AZT, ddC, 3TC), the fragmentation pathways were different from endogenous nucleosides; for AZT, the fragmentation occurred primarily through the elimination of the azido group in the 3'-position (M-H2-N3)-, whereas ddC and 3TC presented more complex fragmentation patterns. For ddC, fragmentation appeared to be dominated by a retro Diels-Alder mechanism (M-CONH)-. For 3TC, the sulfur atom in the sugar moiety provided greater stability to the charge, producing fragments where the charge resided initially in the dideoxyribose (M-C2O2H6)-.

L23 ANSWER 163 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 127:302853 CA
TI Online cleaning HPLC-UV-MS: a tool for analyzing new anti-**HIV drugs** in biological media
AU Lefebvre, Isabelle; Pompon, Alain; Valette, Gilles; Perigaud, Christian; Gosselin, Gilles; Imbach, Jean-Louis
CS Laboratoire de Chimie Bioorganique, U.M.R. C.N.R.S, Univ. Montpellier II, Montpellier, 34095, Fr.
SO LC-GC (**1997**), 15(9), 868, 870, 872, 874, 876
AB The authors used online cleaning high performance liq. chromatog. with UV and **mass spectrometry** detection to study the metabolic pathways and kinetic parameters of new antiviral drugs during incubation in various biol. media. In their studies, they injected crude aliquots into a cleaning precolumn and then transferred the cleaned analytes into an anal. column and chromatographed them. By using sequential detection with a diode-array UV absorbance detector and a **mass spectrometer**, the authors were able to quantify and det. the structures of transient metabolites.

L23 ANSWER 173 OF 188 CA COPYRIGHT 2007 ACS on STN
AN 123:217605 CA
TI Quantification of the anti-**HIV drug saquinavir** by high-speed online high-performance liquid chromatography/tandem **mass spectrometry**
AU Knebel, N. G.; Sharp, S. R.; Madigan, M. J.
CS Dep. Pharmacokinetics Metabolism, Roche Products Ltd., Welwyn Garden City, Hertfordshire, AL7 3AY, UK

SO Journal of Mass Spectrometry (**1995**), 30(8), 1149-56

AB A method is described for the fast routine detn. of the anti-**HIV drug saquinavir** and its pentadeuterated analog [2H5]**saquinavir** in the plasma of healthy volunteers. The method is based on high-performance liq. chromatog. (HPLC)/atm. pressure pos.-ion chem. ionization (APCI) **mass spectrometry**, with a stable labeled form of **saquinavir** (13C6-2H3-15N) as internal std. Automated solid-phase extn. in combination with short-column HPLC and multiple reaction monitoring is employed for high selectivity and sensitivity, and this also permits rapid quantification (the run time per sample is 1.5 min) over the range of 0.4-200 ng mL-1 was excellent accuracy and precision. Greater than 200 samples per analyst per day can be analyzed. This assay methodol. illustrates the versatility of APCI tandem **mass spectrometry**, in conjunction with high-speed HPLC, for the fast routine quantification of drugs in the nanograms per mL range, which is essential for clin. pharmacokinetic studies.

=> log y
STN INTERNATIONAL LOGOFF AT 19:41:53 ON 28 DEC 2007